REMARKS

Applicants note that all amendments and cancellations of Claims presented herein are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG),[1] and without waiving the right to prosecute the amended or cancelled Claims (or similar Claims) in the future.

In the Office Action mailed July 6, 2009, the Examiner indicated that no English translation of the Korean priority document has been provided. The Applicants provide a certified copy herewith.

In the Office Action mailed July 6, 2009, the Examiner indicated that the application is not in compliance with 37 C.F.R. 1.821-1.825 because Figures 1 and 2 lack sequence identifiers. The Applicants provide herewith amended Figures 1 and 2 containing sequence identifiers. Additionally, Applicants provide herewith a substitute Sequence Listing in compliance with 37 C.F.R. 1.821-1.825. As such, the Applicants respectfully request that the objection be withdrawn.

I. The Claims are Directed to Statutory Subject Matter

The Examiner rejects Claims 1-3 under 35 U.S.C. 101 because the claims are allegedly directed towards products of nature. The Applicants respectfully disagree with the rejection. Nonetheless, in order to further the business interests of the Applicants, and without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG), and without waiving the right to prosecute the cancelled claims (or similar claims) in the future, the Applicants have amended Claims 1-3 to recite isolated nucleic acids and proteins. As such, the applicants submit that the claims are directed towards statutory subject matter and respectfully request that the rejection be withdrawn.

II. The Claims are Definite

The Examiner rejects Claim 8 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite. In particular, the Examiner states that Claim 8 is indefinite in the recitation of "production of recombinant glycoprotein with reduced glycosylation". The Applicants respectfully disagree with the rejection. Nonetheless, in order to further the business interests of the Applicants, and without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG), and without waiving the right to prosecute the cancelled claims (or similar claims) in the future, the Applicants have amended Claim 8 to recite that the glycoprotein lacks further sugar-chain synthesis of Man_8 on N-linked glycosylation. As such, the Applicants submit that the claims are clear and respectfully request that the rejection be withdrawn.

III. The Claims are Enabled

The Examiner rejects Claims 1-11 under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement. In particular, the Examiner states that "the specification, while being enabled for an isolated polypeptide having α-1,6-mannosyltransferase activity and comprising the nucleic acid sequence of SEQ ID NO:2 and encoded by a polypeptide of SEQ ID NO:1…does not reasonable provide enablement for any nucleic acid molecule encoding a polypeptide having α-1,6-mannosyltransferase activity…" (Office Action, pgs. 4-5).

The Applicants respectfully disagree with the rejection. Nonetheless, in order to further the business interests of the Applicants, and without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG), and without waiving the right to prosecute the cancelled claims (or similar claims) in the future, the Applicants have amended Claim 1 to recite that homologous nucleic acids are of the *Hansenula polymorpha* strain.

The Applicants submit that they have enabled the presently claimed invention. For example, the α-1,6-mannosyltransferase gene of the CBS4732 strain of *Hansenula polymorpha* has 94 to 97% homology at the genomic level and an average of a 96%

homology at the protein level with additional species of *Hansenula polymorpha* (see references 1 attached hereto). Moreover, the α-1,6-mannosyltransferase gene of the CBS4732 strain has a 97.4% homology to SEQ ID NO. 2 of the present invention (See attached Declaration of Hyun-Ah Kang and supplemental Figure 1). The Applicants submit that they have described the claimed composition structurally (SEQ ID NO:2 and sequences 90% homologous, as well as being a *Hansenula polymorpha* derived polypeptide) and functionally (α-1,6-mannosyltransferase activity) such that a person of ordinary skill in the art would be able to make and use the presently claimed invention.

The Examiner further states that the specification "does not reasonably provide enablement for…ii) an engineered *Hansenula polymorpha* Hpoch2Δ mutant strain…transfected with an expression vector comprising any polynucleotide sequence encoding any sugar-chain modifying enzyme…" (Office Action, pg. 5). The Applicants respectfully disagree with the rejection. Nonetheless, in order to further the business interests of the Applicants, and without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG), and without waiving the right to prosecute the cancelled claims (or similar claims) in the future, the Applicants have amended Claim 7 to recite the sugar-chain modifying enzymes α-1,2-mannosidase, N-acetyl glucosaminiyltransferase I or N-acetyl glucosaminiyltransferase II.

Working data with α-1,2-mannosidase is disclosed in Example 5 of the present specification. The Applicants submit the Declaration of Hyun-Ah Kang, one of the inventors of the present invention. Mr. Kang's declaration describes an additional working example related to N-acetyl glucosaminiyltransferase I (MGAT1) conducted according to the methods of the present application. The present inventors have designed a vector with an active domain of N-acetylglucosaminyltransferase I derived from human and a N-terminal golgi targeting domain (derived from HpOch2 (renamed as "HpOch1" after the present application) and HpOch1 (renamed as "HpOcr1" after present application) of *Hansenula polymorpha*, and ScOch1 and ScKre2 of *Saccharomyces cerevisiae*, respectively), for expressing in the golgi apparatus of *Hansenula polymorpha* at which occurs sugar-chain synthesis (See reference 2 and supplemental Figure 2A). The above vectors were then transfected with HpOch2Δ infected microorganisms were

selected for (see enclosed supplementary Figures 2B and 2C). Moreover, for determining the expression of recombinant glycoprotein, the present inventors analyzed the sugar-chain structure of glycoprotein using Capillary electrophoresis (CE). As shown in supplemental Figure 3, a new peak of $GlcNAC_1Man_5GlcNac_2$ was observed by adding N-acetylglucosamine (dotted line, number 7 of supplemental Figure 3) compared to the strain without MGAT1 (number 3 of enclosed supplemental Figure 3). N-acetyl glucosaminiyltransferase II is very smilar to N-acetyl glucosaminiyltransferase I, and it is clear that N-acetyl glucosaminyltransferase II has a similar effect.

Mr. Kang' declaration and the Supplemental Figures demonstrate that exogenous N-acetyl glucosaminyltransferase I has been expressed in *Hansenula polymorpha* and that recombinant glycoproteins with human glycosylation patterns are expressed in such strain.

Accordingly, the Applicants submit that they have provided sufficient disclosure for one of skill in the art to practice the presently claimed invention. Accordingly, the Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the applicant encourages the Examiner to call the undersigned collect at (608) 662-1277.

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